CLAIMS

We claim:

1. An isolated nucleic acid molecule of SEQ ID NO:1, wherein G is replaced by C at nucleotide 12.

2. The isolated nucleic acid molecule of claim 1 and an isolated nucleic acid molecule of SEQ ID NO:1, wherein the two isolated nucleic acid molecules are forms of a single nucleotide polymorphism in the 5′ region of a thymidylate synthase (TS) gene.

3. A single-stranded nucleic acid probe that hybridizes to the isolated nucleic acid molecule of claim 1, but not to SEQ ID NO:1.

4. The probe of claim 3, wherein the nucleic acid is DNA.

5. The probe of claim 3, wherein the probe is detectably labeled.

6. A diagnostic kit comprising the probe as defined by claim 3, and/or an allele-specific nucleic acid primer of 8-40 nucleotides specifically hybridizes to and detects the molecule of claim 1, and instructions for use.

7. The diagnostic kit of claim 6, wherein the primer is of 12-35 nucleotides.

8. The diagnostic kit of claim 6, wherein the primer is of 17-35 nucleotides.

9. The diagnostic kit of claim 6, wherein hybridization indicates reduced transcriptional activity of the TS gene, and a corresponding decreased risk of developing a disease.

10. The diagnostic kit of claim 6, wherein the disease is cancer or cardiovascular disease.

11. A method for determining whether an individual has or has a heightened predisposition to cancer or cardiovascular disease, comprising:

(a) obtaining a sample from the individual comprising nucleic acid molecules containing a thymidylate synthase gene; and

(b) detecting one or more polymorphisms in the TS gene, wherein

(i) an individual with an 3R/3R construct in the 5' region of the TS gene more likely has or has a heightened predisposition as compared to an individual with a 3R/3RV, 2R/2R, 2R/3R, or 2R/3RV construct;

(ii) an individual with a +6 bp/1494 3' untranslated region polymorphism of the TS gene more likely has or has a heightened predisposition as compared to an individual with a –6 bp/1494 3' untranslated region polymorphism of the TS gene;

(iii) an individual with both the 3R/3R construct in the 5' region and a +6 bp/1494 3' untranslated region polymorphism of the TS gene most likely has or has the highest probability of developing cancer or cardiovascular disease (CVD).

12. The method of claim 11, wherein an individual with the 3R/3R construct in the 5' region of the TS gene has two active USF consensus sequences in each 3R portion, resulting in greater transcriptional activity as compared to a subject with one active USF sequence in either a 2R construct or a variable 3RV construct.

13. The method of claim 11, wherein the detecting step comprises amplifying the portion of the nucleic acid molecule comprising the TS gene.

14. The method of claim 13, wherein the amplifying uses the method of polymerase chain reaction.

15. The method of claim 11, wherein the determining step comprises sequencing the portion of the nucleic acid molecule comprising the TS gene.

16. The method of claim 11, wherein the determining step comprises the use of high throughput screening.

17. The method of claim 11, wherein a 3R construct comprises SEQ ID NO:1 and a 3RV construct comprises SEQ ID NO:1, wherein at position 12, G is replaced by C.

18. The method of claim 17, wherein the replacement of G by C at position 12 is associated with the efficacy of a chemotherapeutic or anti-CVD drug, and wherein if the replacement of G by C at position 12 has occurred, the chemotherapeutic or anti-CVD drug is more efficacious than if the substitution had not occurred.

19. The method of claim 11, wherein the TS gene is derived from bodily fluid of the subject.

20. The method of claim 19, wherein the bodily fluid is blood.